REMARKS

By the present Amendment, claims 28, 32-37 and 45-66 are amended. Also, claims 1-27, 29 and 31 have been cancelled without prejudice. New claims 67-69 are added. Accordingly, claims 28, 30 and 32-69 are pending in the application. Re-examination and reconsideration of the application, as amended, are requested.

Claims previously numbered as claims 49-70 have been amended to be re-numbered as claims 45-66, consistent with the Examiner's indication of the renumbering of those claims.

Rejection Under 35 U.S.C. 112, first paragraph:

Claims 28-30 and 32-66 were rejected under 35 U.S.C. 112, first paragraph. In particular, the Examiner stated that the specification, while enabling for an active protein containing a solidified mixture of glucose oxidase, human serum albumin and a cross-linking reagent, and for use of vapor phase glutaraldehyde to provide non-liquid cross-linking, does not reasonably provide enablement for other embodiments within the scope of the claims. The Examiner further stated that it would be speculation and unpredictable as to other active proteins and non-liquid cross-linking processes that will provide desired results when carrying out embodiments substantially different from working embodiments disclosed in the specification.

With regard to cancelled claim 29, the rejection is moot. With regard to claims 28, 30 and 32-66, this rejection is respectfully traversed, because the patent specification describes several embodiments in addition to embodiments employing glucose oxidase (GOx) and human serum albumin. Moreover, the specification is drafted in a manner that would enable one of ordinary skill in the art with respect to embodiments employing proteins other than GOx and human serum albumin. The specification also describes and enables embodiments employing cross-linking reagents other than vapor phase glutaraldehyde.

For example, the present patent specification describes methods of immobilizing proteins or enzymes (and sensors produced by such methods) for physical and chemical stability over time. (Specification, pg. 1, ll 7-10.) The specification makes it clear that different proteins are used for different sensor environments.

Aspects of the invention, thus, relate to the immobilization of proteins or enzymes in sensors and sensors having such immobilized proteins or enzymes. With respect to one aspect of the invention, the particular protein or enzyme employed is dependent upon the parameter to be sensed (i.e., the sensing environment). With respect to another aspect of the invention, GOx is described as an "example" for a sensing device designed to sense glucose. However, the patent

specification makes it clear that other proteins may be employed for other sensing applications of use.

> "The [protein] matrix 18 may be any of a variety of enzymes, proteins, or the like, that may be employed for sensing. For example, if physiological parameter sensing is desired, one or more proteins may be used as the enzyme. More specifically, if the device is a glucose-sensing device, for example, a combination of glucose oxidase (GOx) and human serum albumin (HSA) may be used concurrently in a solid matrix form to form a sensor matrix protein." (Specification, pg. 3, ll. 3-8.)

Moreover, the present patent specification expressly teaches alternative proteins that may be used in place of GOx and HSA.

> "Although GOx is employed in the embodiment described herein, other proteins and/or enzymes may also be used or may be used in place of GOx, including, but not limited to hexose oxidase, lactate oxidase and the like. Other proteins and/or enzymes may also be used as will be evident to those skilled in the art. Moreover, although HSA is employed in the example embodiment, other structural protein, such as collagen or the like, could be used instead of or in addition to HSA." (Specification, pg. 11, l. 21 ti og, 12, l. 3.)

As further described in the present specification, "[t]hose skilled in the art will understand that the concentration utilized may be varied through experimentation to determine which concentration (and of which enzyme or protein) may yield the desired result.

Furthermore, the present specification describes alternative cross-linking reagents.

> "Although glutaraldehyde is used in the embodiment described above, other cross-linking reagents may also be used or may be used in place of glutaraldehyde, including, but not limited to, an amine reative, homofunctional, cross-linking reagent such as Disuccinimidyl Suberate (DSS). Another example is 1-Ethyl-3 (3-Dimethylaminopropyl) Carbodiimide (EDC), ... Other suitable cross-linkers also may be used, as will be evident to those skilled in the art." (Specification, pg. 12, ll. 11-17).

Thus, it is clear that the specification describes alternative embodiments employing proteins other than GOx and HSA and cross-linking reagents other than glutaraldehyde. It is also respectfully submitted that such alternative embodiments would have been enabled to one of ordinary skill in the art, based on the examples and descriptions appearing in the present specification.

In particular, the patent specification describes processes (with respect to Figs. 2a and 2b) for producing a protein matrix and a solidified protein pellet for a sensor. The processes involve

basic actions that one of ordinary skill in the art would readily be able to apply to any suitable protein or protein mixture to form a solidified protein pellet, once taught to do so by the present specification. (Various protein and enzyme mixtures for sensors are well within the knowledge and understanding of one of ordinary skill in the field of the present invention.) From the teachings of the present specification, the result of forming a solidified protein pellet for a sensor from a variety of different possible protein mixtures and cross-linking reagents would be predictable and non-speculative to one of ordinary skill in the art.

It would be readily apparent to one skilled in the art from reading the present specification (without speculation) that the processes described in the present specification for forming a solidified protein pellet and a sensor containing such a pellet would work with a variety of different protein mixtures and cross-linking reagents. For example, while the overall processes are believed to be novel and non-obvious, it is clear from the present specification, that the processes in Figs. 2a and 2b involve basic steps or activities (such as obtaining a protein mixture, adding a cross-linker, injecting and incubating the mixture in a mold, non-liquid cross-linking, washing and cutting) that one of ordinary skill in the art would readily be enabled to carry out (without speculation and with predictable results) with various protein mixtures.

Moreover, as described above, the present specification offers specific examples of alternative proteins and cross-linking reagents. It would not take undue experimentation or speculation by one skilled in the art to employ alternative proteins and cross-linking reagents (including those that are expressly described in the present specification) in embodiments of the processes of Figs. 2-4 to form a sensor or a solidified protein for a sensor, as described in the present specification. Moreover, based on the teachings provided in the present specification, the results of forming a solidified protein for a sensor would have been predictable to one of ordinary skill in the art for various protein mixtures and cross-linking reagents as described in the present specification. Accordingly, the rejection of claims 28, 30 and 32-66 under 35 U.S.C. 112, first paragraph is respectfully traversed.

Rejection Under 35 U.S.C. 112, second paragraph:

Claims 28-30 and 32-66 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 28, the Examiner stated that the claim is confusing and unclear by requiring a sensor body and an active protein disposed with the sensor body, but not requiring the sensor body to have structure capable of containing the active protein. The Examiner suggested that the sensor body be required to contain a space for containing the active protein. In response,

claim 28 is amended herein to recite that the sensor body has a space for receiving an active protein. Accordingly, it is believed that claim 28 complies with the requirements of 35 U.S.C. 112, second paragraph.

With respect to cancelled claim 29, the rejection is moot. However, the Examiner stated that the term "hardened" in claim 29 is uncertain as to meaning and scope. The Examiner suggested that the term "solidified" be used instead. Accordingly, the claims are amended herein to refer to a "solidified" form. In particular, claim 28 is amended herein to recite that the active protein has a solidified form prior to being disposed within the sensor body. Similar amendments are made to claims 46-64 and 66 for consistency. Accordingly, it is believed that each of claims 28, 46-64 and 66 complies with the requirements of 35 U.S.C. 112, second paragraph.

With respect to claims 32-37, the Examiner stated that the claims are unclear as to how they further limit the sensor of claim 28, because the limitations of the claims 32-37 are process limitations relating to a process of making the sensor. In response, each of claims 32-37 is amended to further clarify that the claim provides a definite limitation, defining the type of active protein used in the claimed sensor. For example, claim 32 is amended herein to further clarify that the active protein is one that has been incubated prior to having been exposed to the non-liquid cross-linking process (instead of reciting that the active protein "is" incubated as a process step). Similar amendments are made to claims 33-36. Accordingly, it is believed that each of claims 33-36 complies with the requirements of 35 U.S.C. 112, second paragraph.

Also with respect to claim 32, the Examiner stated that the phrase "non-liquid cross-linking process" is uncertain as to process steps required for the process. This characterization of claim 32 is respectfully traversed in that it is believed that the present specification describes examples of non-liquid cross-linking processes, for example, with respect to the vapor phase processes described on page 14, line 19 to page 16, line 1. In particular, the patent specification describes procedures for exposing the protein mixture to vaporized cross-linking reagents. However, in an effort to expedite the prosecution of the present application, claim 32 is amended herein to refer to exposing the protein to a vapor phase cross-linking process. Similar amendments are made to dependent claims 33, 34, 36 and 37 for consistency. Accordingly, it is believed that claim 32 complies with the requirements of 35 U.S.C. 112, second paragraph.

With respect to claims 45 and 64, the Examiner stated that the claims are confusing by not having clear antecedent basis for the silicon particles. In response, those claims are amended to include an antecedent basis for the silicon particles. Accordingly, it is believed that each of claims 45 and 64 complies with the requirements of 35 U.S.C. 112, second paragraph.

With respect to claim 46, the Examiner stated that it is unclear as to whether the protein mixture is of different proteins or a mixture of a protein with some other component. In response, it is noted that the patent specification describes embodiments in which the sensor protein matrix 18 may be a variety of enzymes, proteins or the like, where one or more proteins may be used as the enzyme. (Specification, pg. 3, ll. 3-8.) Accordingly, claim 46 is amended herein to clarify the protein *component* of the sensor comprises at least one protein. For consistency, claims 47-53, 63 and 64 are also amended to replace "protein mixture" with "protein component." Accordingly, it is believed that claim 46 complies with the requirements of 35 U.S.C. 112, second paragraph.

With respect to claims 47-52, the Examiner stated that those claims are confusing and unclear by using process limitations and/or requiring a non-liquid cross-linking process, for reasons set forth with respect to claims 32-37. In response, claims 47-52 are amended consistent with the manner in which claims 32-37 are amended (and discussed above). Thus, for reasons as discussed above with respect to claims 32-37, it is believed that each of claims 47-52 complies with the requirements of 35 U.S.C. 112, second paragraph.

With respect to claims 60-62, the Examiner stated that those claims are unclear as to structure reciting "elongated rope-like structure." The Examiner also stated that claim 65 (apparently, claim 61) is unclear with respect to how the cut pieces differ from the pellet and that claim 66 (apparently, claim 62) is unclear as to how a rope-like structure can be semi-cylindrical. In response, claim 60 is amended herein to avoid the use of the phrase "rope-like" and to further clarify that the at least one pellet is configured as at least one elongated structure having a dimension that is elongated relative to its other dimensions. Claim 61, as amended, clarifies that the at least one pellet comprises a plurality of pellets that have been cut from a single, elongated length of protein material. Claim 62 is amended herein to clarify that the *elongated structure* is semi-cylindrical in cross-section. Accordingly, it is believed that each of claims 60-62 complies with the requirements of 35 U.S.C. 112, second paragraph.

With respect to claim 40, the Examiner correctly noted that the claim was inadvertently a duplicate of claim 30. In response, claim 40 is amended herein to be dependent on claim 32 and, thus, is no longer identical to claim 30. Accordingly, it is believed that claim 40 complies with the requirements of 35 U.S.C. 112, second paragraph.

With respect to claims 42, 43, 58 and 59, the Examiner stated that it is unclear as to what constitutes the volume on which the percent by weight per volume is based. In response, claims 42 and 43 are amended herein to clarify that the percentage is based on the weight per volume of the active protein. Claims 58 and 59 are amended to clarify that the percentage is based on the

weight per volume of the combined protein component and cross-linking agent. Accordingly, it is believed that each of claims 42, 43, 58 and 59 complies with the requirements of 35 U.S.C. 112, second paragraph.

Therefore, the rejection of claims 28-30 and 32-66 is respectfully traversed.

35 U.S.C. 102 and 103 Rejections over Patent References:

Claims 28-30, 32-41 and 65 were rejected under 35 U.S.C. 102(e) as being anticipated by Clark, Jr. (USP 6,343,225). Claims 42 and 43 were rejected under 35 U.S.C. 103(a) as being unpatentable over Clark, Jr. Claims 44 and 45 were rejected under 35 U.S.C. 103(a) as being anticipated by Clark, Jr. in view of Blubaugh Jr. et al. (USP 5,964,993). Claims 46-62 and 66 were rejected under 35 U.S.C. 103(a) as being anticipated by Clark, Jr. in view of Liston et al. (USP 4,891,104). Claims 63 and 64 were rejected under 35 U.S.C. 103(a) as being unpatentable over Clark, Jr. in view of Liston et al. and further in view of Blubaugh, Jr. et al. Claims 28-30, 32-43 and 65 were further rejected under 35 U.S.C. 103(a) as being unpatentable over Schulman et al. (USP 6,498,043) in view of Clark, Jr. and further in view of Avameas et al. (USP 4,970,156), Wilkins (USP 5,476,776) or Yamaguchi et al (USP 5,186,808). Claims 44 and 45 were rejected under 35 U.S.C. 103(a) as being unpatentable over Schulman et al. (USP 6,498,043) in view of Clark, Jr. and further in view of Avameas et al. (USP 4,970,156), Wilkins (USP 5,476,776) or Yamaguchi et al (USP 5,186,808) and further in view of Blubaugh, Jr. et al.. Claims 46-62 and 66 were rejected under 35 U.S.C. 103(a) as being unpatentable over Schulman et al. (USP 6,498,043) in view of Clark, Jr. and further in view of Avameas et al. (USP 4,970,156), Wilkins (USP 5,476,776) or Yamaguchi et al (USP 5,186,808) and further in view of Liston et al. Claims 63 and 64 were rejected under 35 U.S.C. 103(a) as being unpatentable over Schulman et al. (USP 6,498,043) in view of Clark, Jr. and further in view of Avameas et al. (USP 4,970,156), Wilkins (USP 5,476,776) or Yamaguchi et al (USP 5,186,808) and further in view of Liston et al. and yet further in view of Blubaugh, Jr. et al. Each of these rejections is respectfully traversed as follows.

In particular, it is respectfully submitted that the claims, as amended herein, recite a sensor or protein for a sensor, including features that are neither described nor suggested by the prior art of record, alone or in combination.

As amended, independent claim 28 recites a sensor comprising a sensor body and an active protein that has a solidified form prior to being disposed with a space in the sensor body and which is received within the space in the sensor body while in solidified form. Also, independent claim 46 recites a "solidified protein material for a sensor," where a combined protein component and cross-linking reagent is solidified into at least one pellet for disposing in

a sensor. Also, claim 65 recites an active protein for disposing in a sensor, the active protein comprising a solidified pellet composed of gluscose oxidase, human serum albumin, and a cross-linking reagent.

In addition, new claims 67-69 further emphasize differences between the claimed invention and the gel-form enzymes described in cited patent references. In particular, new claims 67-69 recite that the solidified form of the active protein (or the solidified pellet is hard enough to maintain its shape without external forces.

None of the cited references describes or suggests a sensor having an active protein that is in a solidified form before being disposed in the sensor body. A sensor (and a sensor protein) that has such a solidified form can provide distinct improvements over the sensors described in the cited patent references.

The Clark Jr. patent describes an implantable glucose sensor that employs an enzyme gel. This type of sensor is described in the background section of the present patent application. In particular, the present patent specification describes problems associated with sensor enzymes in gel form. In particular, it can be difficult to ensure that gel enzymes have filled the volume of a sensor device completely. Voids left in the cavity can adversely affect the stability and sensitivity of the sensor. Moreover, gel enzymes tend to shrink over time and form further voids or spaces in the enzyme cavity of the sensor. (See, e.g., Specification, pg. 4, ll. 1-23.)

The Examiner cited Liston et al as disclosing an enzyme solution in the form of "a bead," citing col. 14, ll. 40-46 of the Liston et al. patent. However, the "bead" that Liston et al. refers to appears to be a non-solid, e.g., liquid bead. The term "bead" is commonly used to refer to a drop of liquid (e.g., a bead of sweat or a bead of blood). Liston et al. describe the formation of an active enzyme membrane layer 602 by applying a "bead" of a solution on the membrane 600 and then compressed to a thin film. The enzyme solution is described by Liston et al. as "a glucose oxidase/bovine serum albumin solution cross-linked with glutaraldahyde." (Liston et al. col. 14, ll. 39-41.) Liston et al. provides no description of any procedure whereby that solution would be formed in a solidified structure. Furthermore, Liston et al.'s teaching of forming a thin film by compressing the bead implies that the bead is not solid, but, instead is a liquid. Accordingly, Liston et al. does not teach or suggest a protein that is solidified before it is placed in the sensor body.

None of the other cited patent references address the above-noted deficiencies of the Clark Jr. and Liston et al. patent references. None of those patent references teach or suggest a sensor protein (or sensor containing the sensor protein) that is solidified before it is received in the sensor body. For example, Schulman et al., Avameas et al., Wilkins and Yamaguchi each

describes a gelatinous material. Furthermore, none of the other patent references were cited by the Examiner for such a teaching. Instead, for example, Blubaugh et al. was cited for disclosing silicone to facilitate the transport of oxygen.

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 06-1447. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 06-1447. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 06-1447.

Respectfully submitted,

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